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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,120	06/14/2001	David Thomas Dudley	5968-01-SMH	5646

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EXAMINER

HUI, SAN MING R

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/868,120

Applicant(s)

DUDLEY ET AL

Examiner

San-ming Hui

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed NOVEMBER 10, 2004 have been entered.

Claims 6-21 are pending.

The outstanding rejection under 35 USC 112, first paragraph is withdrawn in view of the amendments filed NOVEMBER 10, 2004.

The outstanding rejections under 35 USC 102 are withdrawn in view of the amendments filed NOVEMBER 10, 2004.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scherle et al. (The Journal of Immunology, 1998 Oct;161:5681-5686) and McGilvray et

al. (The Journal of Biological Chemistry, 1997; 272(15): 10287-10294) in view of Bridges (WO 98/37881 from the International Search Report).

Scherle et al. teaches a MEK inhibitor, U0126, as effective in inhibiting the production of proinflammatory cytokines, such as IL-1, IL-8, TNF, and prostaglandin E2 (See the abstract and apge 5684, col. 2, first paragraph).

McGilvray et al. teaches the involvement of MAP kinase (MEK) pathway in the activation of monocytic cells during transmigration to inflammatory sites (See the abstract). McGilvray et al. teaches the selective inhibition of MAP kinase by MEK-1 inhibitor, PD98059, being useful for blocking and interrupting the adhesion and recruitments of human monocytes and thereby modulating the inflammatory response (See the abstract and page 10287, col. 2, second paragraph).

The primary references do not expressly teach the active compounds herein to be MEK inhibitors useful for the treatment of arthritis.

Bridges teaches that the active compounds herein are MEK inhibitors (See page 3, line 16 – page 22, line 29). Bridges also teaches the specific MEK inhibitor recited in claim 17 herein as a preferred MEK inhibitor (See page 22, line 24-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis.

One of ordinary skill in the art would have been motivated to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis: the activation of MEK is known to be involved in reducing the inflammatory process, such

as production of inflammatory cytokines and prostaglandin E2, interpretation of adhesion and recruitments of monocytes to the inflammatory sites, in the body. Furthermore, the inhibition of MEK is known to 1) suppress the production and release of pro-inflammatory cytokines such as interleukin-1 β , PGE2, TNF, and interleukin-8; and 2) block and interrupt the adhesion of monocytes to the inflammatory sites. Possessing the teachings of the prior art the skilled artisan would therefore employ any known MEK inhibitors, including those MEK inhibitors of Bridges, to treat arthritis such as rheumatoid arthritis and osteoarthritis, absent evidence to the contrary.

Response to Arguments

Applicant's arguments filed NOVEMBER 10, 2004 averring the herein demonstrated unexpected improvements in MEK inhibition and more desirable pharmaceutical qualities of the herein claimed compounds by citing three articles, have been considered, but are not found persuasive. Among the three articles the applicant cited, Current Pharmaceutical Design article is published in 2004, which is a post filing date reference. The unobviousness has to be established at the time the application is filed. Therefore, arguments directed to the Current Pharmaceutical Design article are not probative evidence for unobviousness. Davies et al. discusses the specificity of various MEK inhibitors, although PD184532 apparently has the highest specificity, it does not expressly teach that the other MEK inhibitors as ineffective *in vivo*. Squires et al. teaches the IC50 of the various MEK inhibitors. Again, the teachings of Squires et al. does not discourage one of ordinary skill in the art to employ MEK inhibitors. It is

noted that various compounds in the same pharmacological class will have a different degree of activities, toxicity such as IC50, and/or specificity to certain enzymes or receptors. Applicant cited references merely teach certain MEK inhibitors have better activities or IC50 than the other MEK inhibitors. Such teachings illustrates that the alleged unexpected difference is merely different in degree, not difference in kind.

Applicant's remarks with regard to PD194352 have been considered, but are not found persuasive. It is not clear how the teachings of the three applicant cited references would lead to the conclusion with regard to PD194352, since the teachings of the Applicant's cited references do not disclose any activities of PD 194352.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-

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0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


San-ming Hui
Primary Examiner
Art Unit 1617